Mechanical Control of Epithelial-to-Mesenchymal Transitions in Development and Cancer.

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Public Summary:
Mechanical force modulates development, influences tissue homeostasis, and contributes to disease. Here, we review literature that addresses how forces induce mechanotransduction pathways to control cell fate, particularly in the context of epithelial-to-mesenchymal transitions that occur during embryonic development and cancer malignancy.

Scientific Abstract:
Mechanical force modulates development, influences tissue homeostasis, and contributes to disease. Forces sculpt tissue-level behaviors and direct cell fate by engaging mechanoreceptors and by altering organization of the cytoskeleton and actomyosin contractility to stimulate mechanotransduction mechanisms that alter transcription. Nevertheless, how force specifically leverages mechanotransduction pathways to control transcriptional regulation of cell fate remains unclear. Here we review recent findings specifically in the context of epithelial-to-mesenchymal transitions that have revealed conserved mechanisms whereby extracellular force, mediated through cell-extracellular matrix and cell-cell junctional complexes, induces transcriptional reprogramming to alter cell and tissue fate. We focus on the interplay between tissue mechanics and the epithelial-to-mesenchymal transitions that occur during embryonic development and cancer malignancy. We describe the adhesion-linked cellular machinery that mediates mechanotransduction and elaborate on how these force-linked networks stimulate key transcriptional programs that induce an epithelial-to-mesenchymal phenotypic transition, thereby providing an overview of how mechanical signals can be translated into a change in cell fate. Expected final online publication date for the Annual Review of Cell and Developmental Biology Volume 32 is October 06, 2016. Please see http://www.annualreviews.org/catalog/pubdates.aspx for revised estimates.